

CLAIMS

We claim:

1. A biodegradable non-toxic cationic lipopolymer comprising a branched polyethylenimine(PEI), a lipid anchor, a biocompatible hydrophilic polymer spacer, and a biodegradable linker which covalently links the branched PEI, the spacer and the cholesterol derived lipid anchor.
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2. The cationic lipopolymer of claim 1, wherein the biodegradable linker is an ester bond.
3. The cationic lipopolymer of claim 1, wherein the lipid anchor is cholesterol or its derivative, a C₁₂ to C₁₈ fatty acid or a derivative thereof.
4. The cationic lipopolymer of claim 1, wherein the biocompatible hydrophilic polymer spacer is polyethylene glycol(PEG) having a molecular weight of between 0.5 to 20K Daltons.
5. The cationic lipopolymer of claim 1, further comprising a targeting moiety selected from the group consisting of transferrin, asialoglycoprotein, antibodies, antibody fragments, low density lipoproteins, interleukins, GM-CSF, G-CSF, M-CSF, stemcell factors, erythropoietin, epidermal growth factor (EGF), insulin, asialoorosomucoid,
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mannose-6-phosphate, mannose, Lewis^X and sialyl Lewis^X, N-acetyllactosamine, galactose, lactose, and thrombomodulin, fusogenic agents such as polymixin B and hemagglutinin HA2, lysosomotropic agents, and nucleus localization signals (NLS) .

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6. The cationic lipid of claim 5 wherein the targeting moiety is galctose or lactose.

7. The cationic lipopolymer of claim 1, wherein molar ratio of the branched PEI to the lipid anchor is preferably within a range of 1:1 to 1:20.

8. A biodegradable non-toxic cationic lipopolymer comprising a branched polyethylenimine(PEI) having an average molecular weight of 600 to 1200 Daltons, a lipid anchor, biocompatible hydrophilic polymer spacer, and a biodegradable linker which covalently links the branched PEI, the spacer and the cholesterol derived lipid anchor.

9. The cationic lipopolymer of claim 8, wherein the biodegradable linker is an ester bond.

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10. The cationic lipopolymer of claim 8, wherein the lipid anchor is a cholesterol, a C₁₂ to C₁₈ fatty acid or a derivative thereof.

11. The cationic lipopolymer of claim 8, wherein the biocompatible hydrophilic polymer spacer is polyethylene glycol(PEG) having a molecular weight of between 0.5 to 20K Daltons.

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12. The cationic lipopolymer of claim 8, further comprising a targeting moiety selected from the group consisting of transferrin, asialoglycoprotein, antibodies, antibody fragments, low density lipoproteins, interleukins, GM-CSF, G-CSF, M-CSF, stemcell factors, erythropoietin, epidermal growth factor (EGF), insulin, asialoorosomucoid, mannose-6-phosphate, mannose, Lewis^X and sialyl Lewis^X, N-acetyllactosamine, galactose, lactose, and thrombomodulin, fusogenic agents such as polymixin B and hemagglutinin HA2, lysosomotropic agents, and nucleus localization signals (NLS) .

13. The cationic lipid of claim 12 wherein the targeting moiety is galctose or lactose.

14. The cationic lipopolymer of claim 8, wherein molar ratio of the branched PEI to the lipid anchor is preferably within a range of 1:1 to 1:2.

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15. A biodegradable non-toxic cationic lipopolymer comprising a branched polyethylenimine(PEI) having an average molecular weight of 1800 to 25000 Daltons, a

lipid anchor, biocompatible hydrophilic polymer spacer, and a biodegradable linker which covalently links the branched PEI, the spacer and the cholesterol derived lipid anchor.

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16. The cationic lipopolymer of claim 15, wherein molar ratio of the branched PEI to the lipid anchor is preferably within a range of 1:1 to 1:5.

17. The cationic lipopolymer of claim 15, wherein the biodegradable linker is an ester bond.

18. The cationic lipopolymer of claim 15, wherein the lipid anchor is a cholesterol, a C₁₂ to C₁₈ fatty acid or a derivative thereof.

19. The cationic lipopolymer of claim 15, wherein the biocompatible hydrophilic polymer spacer is polyethylene glycol(PEG) having a molecular weight of between 0.5 to 20K Daltons.

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20. The cationic lipopolymer of claim 15, further comprising a targeting moiety selected from the group consisting of transferrin, asialoglycoprotein, antibodies, antibody fragments, low density lipoproteins, interleukins, GM-CSF, G-CSF, M-CSF, stemcell factors, erythropoietin, epidermal growth factor (EGF), insulin, asialoorosomucoid, mannose-6-phosphate, mannose, Lewis^X and sialyl Lewis^X, N-acetyllactosamine,

galactose, lactose, and thrombomodulin, fusogenic agents such as polymixin B and hemagglutinin HA2, lysosomotropic agents, and nucleus localization signals (NLS) .

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21. The cationic lipid of claim 20 wherein the targeting moiety is galctose or lactose.

22. A pharmaceutical composition comprising a bioactive agent and a biodegradable non-toxic cationic lipopolymer comprising a branched polyethylenimine(PEI), a lipid anchor, biocompatible hydrophilic polymer spacer, and a biodegradable linker which covalently links the branched PEI, the spacer and the cholesterol derived lipid anchor.

23. The composition of claim 22, wherein the biodegradable linker is an ester bond.

24. The composition of claim 22, wherein the lipid anchor is a cholesterol, a C₁₂ to C₁₈ fatty acid or a derivative thereof.

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25. The composition of claim 22, wherein the biocompatible hydrophilic polymer spacer is polyethylene glycol(PEG) having a molecular weight of between 0.5 to 20K Daltons.

26. The composition of claim 22, further comprising a targeting moiety selected from the group consisting of transferrin, asialoglycoprotein, antibodies, antibody fragments, low density lipoproteins, interleukins, GM-CSF, G-CSF, M-CSF, stemcell factors, erythropoietin, epidermal growth factor (EGF), insulin, asialoorosomucoid, mannose-6-phosphate, mannose, Lewis^X and sialyl Lewis^X, N-acetyllactosamine, galactose, lactose, and thrombomodulin, fusogenic agents such as polymixin B and hemagglutinin HA2, lysosomotropic agents, and nucleus localization signals (NLS) .

27. The composition of claim 26 wherein the targeting moiety is galctose or lactose.

28. The composition of claim 22, wherein molar ratio of the branched PEI to the lipid anchor is preferably within a range of 1:1 to 1:20.

29. The composition of claim 22 wherein said bioactive agent is a nucleic acid, protein or an anionic drug.

30. The composition of claim 29, wherein the charge ratio of the cationic lipopolymer and the nucleic acid (+/-) is within a range of 5:1 to 1:1.

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31. The composition of claim 29, further comprising a helper lipid.
32. The composition of claim 31, wherein the helper lipid is a member selected from the group consisting of dioleoylphosphatidylethanolamine(DOPE), oleoylpalmitoyl-phosphatidylethanolamin(POPE), diphyanoylphosphatidylethanolamin (diphyanoylPE), disteroyl-, -palmitoyl-, -myristoylphosphatidylethanolamine and 1- to 3-fold N-methylated derivatives thereof.
33. The composition of claim 31, wherein the molar ratio of the cationic lipopolymer and the helper lipid is within a range of 4:1 to 1:2.
34. A method of delivering a bioactive agent into a warm blooded animal, comprising administering a effective amount of the composition comprising a bioactive agent and a biodegradable non-toxic cationic lipopolymer comprising a branched polyethylenimine(PEI), a lipid anchor, biocompatible hydrophilic polymer spacer, and a biodegradable linker which covalently links the branched PEI, the spacer and the cholesterol derived lipid anchor to the animal under conditions wherein said composition enters said cells, and the bioactive agent of said composition is released.
- 20 35. The method of claim 34 wherein the administration is local or systemic.